Co-infections: potentially lethal and unexplored in COVID-19

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Respiratory viral infections predispose patients to co-infections and these lead to increased disease severity and mortality. Most fatalities in the 1918 influenza outbreak were due to subsequent bacterial infection, particularly with *Streptococcus pneumoniae*.[1] Poor outcomes in the 2009 H1N1 influenza pandemic were also associated with bacterial co-infections, although few studies captured these data.[2]

Despite the proven importance of co-infections in the severity of respiratory diseases, they are understudied during large outbreaks of respiratory infections. Zhou and colleagues[3] showed that in the current coronavirus disease 2019 (COVID-19) pandemic, 50% of patients with COVID-19 who have died had secondary bacterial infections, and Chen and colleagues[4] have recorded both bacterial and fungal co-infections. Although 71% of the admitted patients with COVID-19 received antibiotic drugs, no information is available on the antimicrobial sensitivities of the organisms that were identified, or on the type and duration of antimicrobial treatment. Chronic obstructive pulmonary disease (COPD) is a risk factor for severe COVID-19 disease and many patients with COPD will have underlying chronic bacterial infections before severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, but this important information is not being reported. More data on co-infections are urgently required to establish their importance in COVID-19 severity and mortality.

Diagnosing co-infections is complex. The organism itself might be carried by the patient before the viral infection, might be part of an underlying chronic infection, or might be picked up nosocomially. In the UK, National Institute for Health and Care Excellence (NICE) treatment guidance for severe acquired pneumonia is broad-spectrum antibiotic co-amoxiclav plus a macrolide to cover atypical organisms. Currently, antibiotic use is high (74·5%) among patients with COVID-19 who are admitted to intensive care units, rendering culture-based microbiological testing less sensitive. Patients with COVID-19 are kept on invasive mechanical ventilation for a long time (mean 9·1 days [SD 5·5]), increasing chances of hospital and ventilator acquired infections. Hence, early diagnosis of co-infection is required, preferably using methods capable of detecting a broad range of potential pathogens and antimicrobial resistances, with subsequent monitoring for infection development. To accurately diagnose and study co-infection in COVID-19, patients should be recruited on admission to intensive care units and sampled longitudinally throughout the disease course using culture-independent techniques capable of identifying complex mixed infections without previous target selection, such as whole-genome metagenomics.[5] Such a study would provide valuable surveillance data on the pathogens causing co-infections and antimicrobial resistance in the intensive care setting, thereby helping inform antibiotic prescribing policy.

Rapid characterisation of co-infection is essential in the management and treatment of the most severe COVID-19 cases, could help to save lives, and will improve antimicrobial stewardship throughout the course of the pandemic.

DB has received research grants from MedImmune, outside of the submitted work. All other authors declare no competing interests.

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Published **Online**
April 24, 2020
https://doi.org/10.1016/S2666-5247(20)30009-4

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For data from the **International Severe Acute Respiratory and Emerging Infection Consortium** see http://ISARIC.tghn.org